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THE VASCULAR BASIS OF SOME NODULAR ERUPTIONS OF THE LEGS.

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THE condition to which I shall confine my remarks has been defined by Montgomery, O'Leary and Barker (1945) as involving

> " . . . primarily the legs, characterised by the presence of nodules, and sometimes by ulceration, and which are associated with varying degrees of involvement of the blood-vessels and fibrosis."

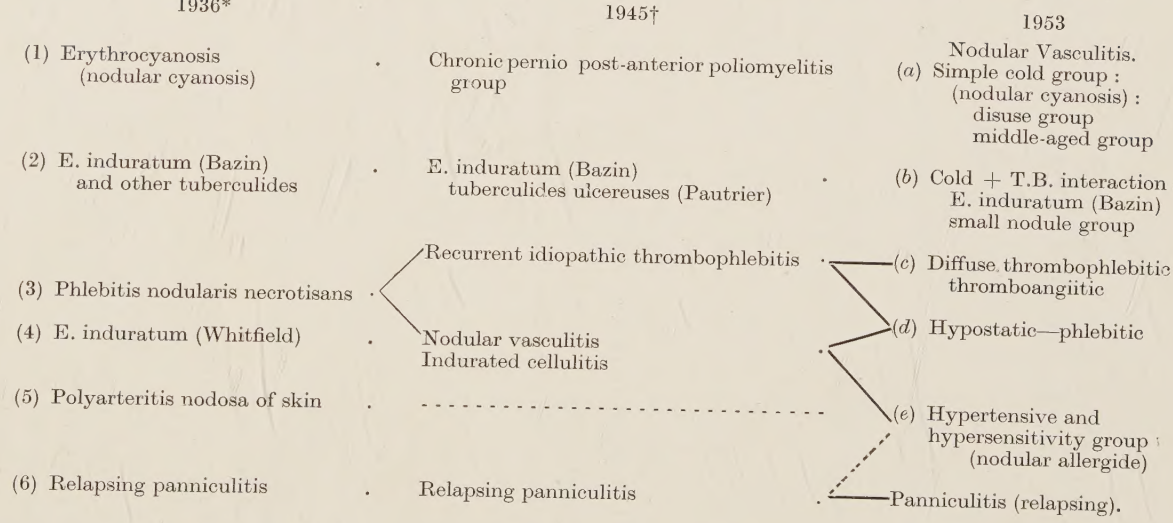
This group has given rise to a great deal of confusion in the literature since Bazin's first description, in 1858, of *érythème induré des scrofuleux*. It is paradoxical that it was only later when the tubercle bacillus had been discovered, that the scrofulous association was questioned, on failure to recover the bacillus from the lesions. Audry (1898) and Galloway (1899, 1913) were probably the first to dispute this, but the name of Whitfield is particularly linked with cases which are not tuberculous.

The term nodular vasculitis was introduced by Montgomery, O'Leary and Barker (1944, 1945) who remark that " our concept of nodular vasculitis corresponds well with the description given by Galloway and Whitfield in several articles." This term has gained ground, particularly in the U.S.A., as an alternative name for Whitfield's erythema induratum, but there has been a wider reluctance in England to change an old lamp for a new one unless its advantages were manifest. Bettley (1950) has expressed this view. Michelson (1952) and Irgang (1953) have recently discussed nodular vasculitis, the latter reporting two further cases. Manifestly, however, the limits of the condition are not yet well-defined.

At the same time other associated conditions have become separated from Bazin's disease. These are concerned with a broad group of allergic reactions, other tuberculides, and abnormal responses to cold. The growth of these ideas is referred to in Table I.

TABLE I.—*Nodular Lesions of the Legs.*

Simplified Classification of Main Types (excluding Erythema nodosum).


1936*
1945†
1953
Nodular Vasculitis.
(1) Erythrocyanosis (nodular cyanosis)
Chronic pernio post-anterior poliomyelitis group
(a) Simple cold group : (nodular cyanosis) : disuse group middle-aged group
(2) E. induratum (Bazin) and other tuberculides
E. induratum (Bazin) tuberculides ulcereuses (Pautrier)
(b) Cold + T.B. interaction : E. induratum (Bazin) small nodule group
(3) Phlebitis nodularis necrotisans
Recurrent idiopathic thrombophlebitis
(c) Diffuse thrombophlebitic thromboangiitic
(4) E. induratum (Whitfield)
Nodular vasculitis Indurated cellulitis
(d) Hypostatic—phlebitic
(5) Polyarteritis nodosa of skin
(e) Hypertensive and hypersensitivity group : (nodular allergide)
(6) Relapsing panniculitis
Relapsing panniculitis
Panniculitis (relapsing).

* Before Telford (1937).

† Montgomery *et al.* (1945).

MATERIAL.

This study evolved as an enquiry regarding the clinical appearances of lesions which appeared histologically to have their basis in a reduction of their arterial blood supply or venous return, or both. Forty-two such sections were collected which related to nodular conditions of the legs, and these patients were studied clinically; among them were 25 personal cases, and a further 13

patients were seen on whom no biopsies were performed during the time of this review.

The patients have been seen over a period of three years, but it is salutory to reflect that changes in this group of conditions may be so slow that it is little enough time to form any conclusions of value. The subject is complex, involving a number of physiological processes whose mechanism is obscure. We have first tried to establish some clinical patterns among these patients and to discover common factors affecting similar groups ; first then, are fifteen of our patients whose eruption was obviously related to the influence of cold.

Nodular Lesions Associated with the Action of Cold.

The existence of nodular lesions on the legs due to the action of cold is well recognised. We can, within the limits of our small series, distinguish two quite distinct varieties. The first kind occur simply with the effect of cold and are seen in three groups of patients : —

(i) Young women, tending to obesity or having recently increased in weight, but otherwise healthy (11 cases).

(ii) Women of young to middle age with legs affected by poliomyelitis, rheumatoid arthritis or other immobilizing disease producing substitution of muscle by fat and vascular atony (2 cases).

(iii) Women not necessarily obese, at about menopausal age. These patients may have suffered previously from chilblains, acrocyanosis or Raynaud's phenomenon, or these may develop at the same time (2 cases).

It is of interest that Jepson (1951), dealing with Raynaud's phenomenon, has separated from the main body of cases a group occurring in middle-aged females and having an association with rheumatoid disease.

The young women who suffer from these nodules have often had cold hands and feet but rarely chilblains or Raynaud's phenomenon. The nodules occur with erythrocyanosis—of which they often represent an acute form—or scattered along the backs of the calves and on the lower parts of the legs. The nodules themselves are painless and often arise about 24 hours after some unaccustomed exposure to cold. At first bright pink in colour, they become purple in the course of time and with slight warming, when they tend also to be irritable. They may be grouped in a crescent or horseshoe-shape, the periphery being pink, the centre purple. Sometimes more superficial nodules occur, resembling chilblains or erythema iris, with a characteristic triple-hue (cyanotic centre, pallor, pink edge). On vitropression the purple area remains, though paler, and small " cayenne-pepper " spots (capillary tufts) occur in the pink areas. Follicular perniosis and hypertrichosis may also occur. There are no signs or indications pointing to active or even quiescent tuberculosis. Ulceration is rare except superficially or at sites of friction.

The similarity of these nodules occurring either alone, with erythrocyanosis, or in limbs with disuse atrophy ; the absence of any accompaniment of general ill-health ; the relatively benign course ; the favourable response to continued warmth ; are all in favour of the identity of the group and its relationship to cold.

In 1894, when women's legs were better covered than they are today, Corlett (1895) described similar lesions on the hands and feet, mentioning the horse-shoe-shaped patches. Haxthausen (1930) has described the cayenne-pepper spots and also has stressed the various (and varying) areas of the female body that are most susceptible to the reaction of cold. It is to McGovern and Wright (1941), however, that we owe the modern conception of a diffuse pernio-like condition affecting the legs. Several years previously Telford, in a series of papers (1931, 1933, 1937) had emphasised the identical nature of erythrocyanosis and chronic pernio nodules in the legs of patients who had suffered from poliomyelitis, and mentioned the occurrence of these lesions in limbs with an excessive deposit of fat, or in florid persons. The importance of humidity and convection as provoking factors is well known.

Nodules Associated with the Action of Cold and in Tuberculous Patients.

Sometimes an eruption differs from the foregoing by becoming more persistent in summer, by ulcerating freely, or by an association with periodic attacks of ill-health, loss of weight, and even with overt signs of tuberculous disease such as pleurisy, iritis or the presence of acknowledged tuberculides. The influence of cold cannot be discarded ; the onset is invariably in winter, and there is a frequent association with other forms of cold intolerance and, inconstantly, with erythrocyanosis.

(i) *Large-nodule group.*—These patients, of similar age to those in the previous group, also have similar large nodules on the backs of their calves. In the early stages the differentiation may be difficult. The points that seem to be of importance clinically are mentioned above. In one of these patients, in whom the nodules and ulcers were associated with papulonecrotic tuberculides at the onset and, later, with attacks of iritis, the nodules have remained healed for nine months from autumn to summer following a course of isonicotinic acid hydrazide, having previously persisted through several winters. Here the tuberculous factor seems evident.

(ii) *Small-nodule group.*—We have seen three patients in whom the nodules were small, purple, persistent and occurring around the lower parts of the legs and feet rather than the calves. There was little or no evidence of hypostasis. The relationship to cold and to tuberculosis was the same as in the foregoing group. Our patients were thin, and not entirely well. Tuberculous adenitis

had occurred in all, and the Mantoux reaction was strongly positive. The lesions did not heal quickly on bed rest. This group approximates to the description of Philipson's "phlebitis nodularis necrotisans" (1901) (in two cases of which he cultured the tubercle bacillus) and to the nodular tuberculides of the French school.

The determining factor in these cases is probably a pre-existing area of venous stagnation or capillary dilatation. That tuberculosis, and to a less extent syphilis, more readily exhibit their effects in such predisposed tissue is undoubted. Haxthausen (1930) has discussed this fully.

These patients have a background of unusual reactivity to cold, varying evidence of tuberculous infection, some manifestations of ill-health, and an ulcerating, nodular eruption which may at first resemble the previous group (Bazin's disease) or may consist of smaller, harder nodules occurring about the small superficial veins. What criteria can we establish for tuberculosis being a cause in any particular case ? Those sometimes described as necessary are scarcely helpful. Positive bacteriological findings in the lesion are rare, some would say they denote little. Tuberculides seldom confess their parentage in their histology, which may not even show a tuberculoid picture ; a strong tuberculin skin reaction does not establish pathogenicity in respect of the lesions. Proof, therefore, is difficult to obtain. But the presence of other tuberculides and an immediate and lasting response to isonicotinic acid hydrazide therapy will be very suggestive. There may well exist all gradations of lesions from a frank scrofuloderma, through a state of transient bacillaemia involving an embolic lodgement in areas of vascular stasis, to one of non-specific peripheral vascular reactivity determined by cold or stasis and in some way intensified by tuberculous disease. The bacillus, indeed, whether attenuated or otherwise, may well be able to excite a peripheral vascular reaction on its own, but seems to prefer a suitable focus ready-made. It takes possession when the door is left ajar. The question resolves into what part, if any, the tuberculous process plays in a given lesion, even if the disease is active in the patient. One cannot afford to be too sceptical. A case shown by Montgomery, O'Leary and Brunsting (1944) as "nodular vasculitis," six months later developed hypersensitivity to tuberculin and histologically proved tuberculous cervical adenitis.

Erythema Nodosum.

In its usual form, erythema nodosum presents little difficulty in diagnosis and shows quite a different histological picture, without the vascular changes of the other groups. I shall not discuss it here.

Erythema nodosum-like lesions occur which are more difficult. For instance, some patients with hilar gland enlargement and a negative Mantoux reaction

may show an eruption of large, sparse nodules of slower evolution than erythema nodosum and lasting for some months without undergoing any of the usual colour-changes of resolution. It was reported by Graveson (1942) that such cases showed sarcoid-like changes microscopically, but Wahlgren and Löfgren (1949) deny this, and the one case we have had showed a non-specific picture.

The "chronic" forms of erythema nodosum, such as those occurring with meningococcal fever, are seldom seen nowadays, and should perhaps be classed as "nodular allergides". Other lesions labelled "erythema nodosum" have, in some of our cases, been the initial manifestations of a thromboangiitic nodular vasculitis.

Phlebitic and Thrombotic Group.

In 18 patients the major factor appeared to relate either to a defective venous return or to episodes of thrombosis or thrombophlebitis, chiefly affecting the vessels of the legs but occasionally those elsewhere. Our cases fall into three groups: —

(i) Those in which hypostasis and venous congestion form the main clinical picture.

(ii) Those shewing a more diffuse thrombophlebitis.

(iii) Thromboplebitis in young or middle-aged men (a group which I believe to have a special significance).

(i) *Hypostatic group.*—These cases have been separated from Bazin's disease for a considerable time. Galloway's second case (1913) of a woman aged 36 who had had recurrent nodules for five years, worse in proportion to the amount of housework she did, and disappearing on rest, is a case in point. This group corresponds both with Whitfield's cases and with what Savill called "erythema induratum hypostaticum".

In 9 cases there was evidence of hypostasis, such as aching or a feeling of heaviness of the legs, oedema of the ankles, local purpura and capillaritis, a past history of deep thrombophlebitis, repeated attacks of phlebitis and periphlebitis, or plaques of sclerosis on the lower part of the leg. The age at onset is from 35–60 years in women, the average being 47; and from 30–45 in men.

The nodules seldom ulcerate but resolve slowly with fibrosis; they have a marked bluish-purple colour after the initial inflammatory stage is passed. In some cases there is a reticulate appearance on the legs, in others a persistent irregular sclerosis which acts as the centre of recurrent exacerbations of nodules or attacks of periphlebitis with surrounding inflammation.

In 4 cases a deep thrombophlebitis had occurred some years previously and had been confined to one leg; this leg was predominantly or solely affected.

In 3 others cold appeared to be an additional factor. One patient had had a thyroidectomy the previous year and she manifested an increasing intolerance

to cold as well as oedema of the ankles with the onset of a myxoedematous state. In 2 others there was some hypertension. Support by firm bandaging or elastic stockings often, but not always, controlled the eruption. Lesions disappeared quickly on rest. In another, frequent trials of unilateral support were successful but the nodules on both legs cleared up with bed rest.

Thus, most of the patients had had either thrombophlebitis or an added factor of hypertension or cold intolerance. It seems that simple hypostasis alone seldom causes these symptoms.

(ii) *Thrombophlebitic group.*—In 5 cases this phlebitic process was more widespread, more persistent and associated with more profound symptoms.

A woman of 38 had for seventeen years suffered from recurrent nodules on the legs, intensely painful, reddish-blue and occasionally ulcerating. They were worse in the summer. She had had phlebitis of her right saphenous vein eight years ago, a cerebral vascular accident six years ago and a pulmonary infarct with pleurisy four years ago. She showed an intense reticulate venous livedo of both legs and a few scars of old ulceration. There was much irregular fibrosis. Nodules continued to erupt when she was in bed ; supporting one leg with bandages made this leg more painful. Nodules also developed on the thigh and arm and some of the lesions were disposed along veins. She had an accelerated clotting time and an E.S.R. of 30 mm. per hour.

In a second patient, a man of 32, the nodules were associated with chilblains during the last war, then oedema of the ankles, reactivity of old tuberculous cervical glands, a pleural effusion, and an eventual picture of thrombophlebitis migrans.

This group is distinguished by the combination of frequent recurrences of nodular lesions, a more widespread distribution, involvement of veins giving rise to linear lesions or a reticulate livedo, and fibrosis rather than ulceration. The patients are often ill but the illness is seldom well-defined. Small- or large-vein thromboses may occur in other parts of the body, and the nodules are more painful in the summer. Moreover, these continue to appear while in bed. (Since they are presumably associated with attacks of small-vein thrombosis, this is understandable).

Many difficulties occur in the diagnosis of this group, and it is not easy to decide how closely to limit it. On the one hand, some patients may suddenly develop symptoms of arterial involvment and instead of calling the condition " thrombophlebitis migrans " we now call it " thromboangiitis obliterans ". This change may be long delayed. On the other hand there may be an association with tuberculosis in more than the two cases quoted above. Of two more doubtful cases, the disease in one appeared to clear after control of a fungus infection of the toes. There may not be much significance in this, though the association has aroused interest from time to time, and was at one time emphasised by Thompson (1944).

The diagnosis may be difficult, the prognosis uncertain. Distant thrombosis or arterial involvement may suddenly occur ; toxaemia, cerebal accidents

and the spread of tuberculosis are additional risks. Ruiter, however, (personal communication, 1953) has had some cases that have cleared up completely.

(iii) *Widespread venous and arterial involvement (thromboangiitis).*— Finally, there are those patients who have come to present unmistakable signs of arterial disease. Long periods of phlebitis or the recurrent eruption of nodules looking like—and often labelled as—erythema nodosum may precede the involvement of the arterial system by many years. Men are most commonly affected, uniquely in the whole series.

A hospital porter gave a 10-year history of small, painful nodules recurring on his left leg, then the right leg and the thighs. These were alternately diagnosed as phlebitis and erythema nodosum according to their appearance. He suffered from various intercurrent diseases. A diagnosis of thromboangiitis obliterans was finally made, and sympathectomy performed.

In these cases, also, the condition is worse in summer, perhaps because of increased demands on the blood supply. The signs of arterial vascular disease are present (shiny skin of the toes, nail dystrophy, loss of hair on the back of the leg, cramps, claudication, poor or absent peripheral pulses, poor temperature response, slow or mottled reactive hyperaemia). The nodules in this group are often characteristic, a feature which Sweet has pointed out (personal communication, 1950). They are small, bright red, arising on a background of shiny or mottled skin, often situated on the sides of the feet, and they do not ulcerate.

In senile obliterative arteritis the same features may be seen.

Relatively little is known about the reactivity of veins: Franklin (1937) has assembled together most of the existing information. It is possible that damage to the vessel wall and stasis may be responsible for the phlebitic nodules, seen not only in this group but in the "cold" group also. Perhaps tuberculosis provides an added toxic factor.

The increase in symptoms in hot weather may be related to the rise in capillary pressure that occurs as a result of arteriolar dilatation (Lewis, 1924; Boas, 1922; Landis, 1930) or to defective venous return and an increased blood flow.

It is striking that in no fewer than 10 out of our 18 patients there was reference to a neurotic background (this was also present in Whitfield's cases). Stoker (1952) and others have referred to the part played by emotion in venous spasm. Cannon and Mendenhall (1914) produced persistent reduction in the blood clotting time in cats by inducing nervous excitement in them.

Hypersensitivity and Hypertensive Group.

We have in our series 7 patients in whom the clinical pictures were quite distinct from those preceding.

(i) Of the 7, 5 patients had a considerable degree of hypertension ; 2 of these also had diabetes and 1 suffered from gout. There was a preceding single episode of phlebitis in 2 cases. The onset of the eruption was abrupt, its course usually continuous, persistent ulceration occurring in 2 of the 5 cases. As well as nodules, there were erythematous or papular lesions and purpuric or haemorrhagic blisters, bursting to form ulcers. The bright pink or livid colour, warmth and tenderness of the nodule is in contrast to those in the preceding groups. The average age of onset was 60 years.

(ii) There were 2 cases without hypertension but with evidence of a hypersensitivity state. These correspond to the " nodular allergide " group and would be better represented were their dermatological manifestations less diverse and more consistently nodular. A severe example of this was provided by a man of 45 whose acute purpuric nodular eruption, associated with joint pains, albuminuria and fever, terminated in death. Post-mortem examination led to a final diagnosis of polyarteritis nodosa.

A much more benign form is represented by a man of 48 years who had a five-weeks history of an eruption of small, purple-red nodules on legs and feet with purpuric spots and some patchy erythema. Removal of a septic tooth was followed by their disappearance after they had persisted for two months. The white cell count showed, initially, 9,200 polymorphs per cmm., dropping to normal later. He remained well a year later.

These cases, one malignant and one benign, emphasise the extremes of clinical course that may occur. Both may be regarded as " nodular allergides " and the sudden improvement in the second case, after tooth extraction, may be suggestive of (although not proof of) a bacterial cause.

The variability of these eruptions is their characteristic. The nodules are purplish or bright red—or even purpuric—and frequently ulcerate. They are usually small. As well as nodules, urticarial lesions, purpura or pustules may occur. The picture, in fact, may be bizarre in the extreme. Joint pains, haematuria, albuminuria and signs of widespread involvement of the vascular system may be seen in severe cases. When apparently confined to the skin, this group has been given a variety of names : *polysymptome* (Gougerot) ; allergic (or necrotising) arteriolitis ; polyarteritis nodosa of the skin ; and so on. Each name overlaps the others to some extent, and each embraces a wide group of cases. They have been discussed recently by Ruiter (1953) and by Marshall and Pepler (1953). We should not forget the more sinister import of signs of generalised vascular involvement. Cases of polyarteritis nodosa are not always fatal, and though I think it is a mistake to attach this name to the lesions localised to the skin, we should not forget the greater disease while watching the less.

The vascular reactions that form the basis of these lesions are probably called

into play by a wide variety of different agents, such as bacterial and non-bacterial antigens, drugs, viruses, trauma and physical agents ; they represent a final common denominator occuring at slightly different levels in the vascular tree. It is striking how often some evidence of chronic infection can be found, and the suggestion that the picture represents a reaction to invasion of the skin from within has much to commend it.

Some observers (Zeek, 1952) believe that a generalised " hypersensitivity angiitis " can be distinguished from polyarteritis nodosa.

Diagnosis.

The chief diagnostic features of each main group are summarised in Table II. The nodules themselves are rarely specific in appearance and must be assessed in relation to collateral findings both of a general and local nature, constitutional disturbances, and foci of infection. Laboratory investigations and the use of special techniques as an aid to diagnosis are of more limited value than might be expected.

It is worth while drawing attention again to the preponderance of male patients in the group showing nodules with signs of obliterative vascular disease and their rarity in the other groups.

There are a few further points of clinical interest that may sometimes be of assistance : Ulceration is less likely to occur where the causative mechanism operates slowly and over a length of time, rather than suddenly and with explosive force, and is therefore more commonly met with in the hypersensitivity group ; however, caseation and liquefaction of fat may also lead to ulceration. Biopsy wounds heal badly in the patients with phlebitic lesions or with obliterative arteritis. In the latter condition erythematous macules and a blotchy erythema may occur, especially on the dorsa and sides of the feet, and commonly enough to be of some value in diagnosis. The characteristic colour changes and the pain of obliterative vascular disease may also be present in these patients and the only other nodules which are uniformly painful are those in the phlebitic group. In searching for evidence of a more widespread involvement of the vascular tree, we are sometimes apt to forget that the retina offers us a direct observation of the small arteries. As to the veins, a past attack of thrombophlebitis of the leg or a pulmonary infarct may be disguised by the patient under some euphemism which may deceive the unwary.

Finally, if two factors appear to co-exist, a therapeutic test may be of some value. Rest in bed, excellent treatment though it is for the majority of patients with these eruptions, is far from being diagnostically specific ; the warmth counteracts the effect of cold, recumbency that of hypostasis, relaxation that of hypertension ; thrombophlebitic nodules alone seem to resist its effect, but supporting bandages, protection from cold and other such measures may, if

Table II.

	Cold (simple).	Cold + TB.	Hypostasis and phlebitis.	(*a*) Thrombophlebitis. (*b*) Thromboangiitis.	(*a*) Hypertensive. (*b*) Hypersensitivity.
Nodules	Rather large	Small and hard, or large, indurated	Irregular plaques : sclerosis	Rather small ; linear	Varied.
Average age (onset)	23	25	45 (F.) 34 (M.)	(*a*) 43 (*b*) 38	(*a*) 60 (*b*) 46
Sex	F.	F.	F. M.	(*a*) F. (*b*) M.	(*a*) F.
Other signs	Erythrocyanosis	TB.	(cold)	(cold : phlebitis)	metabolic diseases ; bacterial infection, etc.
Ulceration	—	+	(sclerosis)	sometimes in (*a*)	++ (bullae, purpura)
E.S.R. rise	—	+	— (+ in attacks)	— (+ in attacks)	+
Response to :					
Bed rest	+	+	+	—	+
Leg support	±	±	+	—	±
Antibiotics	—	—	±	±	+ (some cases)

employed singly, counteract the causative mechanism and help to elucidate the factors concerned.

I am altogether aware of the considerable gaps in this account and do not myself accept it as in any way definitive or final. As Montgomery has said, "We do not know what nodular vasculitis is" and in the complexities of research and investigation that surround all aspects of this subject, it remains true that "each case of nodular vasculitis should be considered individually and most painstakingly and unhurriedly evaluated" (Michelson, 1952).

Summary.

1. Forty-two patients presenting with nodular eruptions of the legs have been studied clinically and histologically. In all of these the histology showed predominantly vascular changes.

2. In fifteen patients the eruption was associated with cold, and with no other apparent cause. Clinically, these were regarded as nodular forms of erythrocyanosis.

3. In three patients a persistent eruption of small nodules occurring around the feet and lower parts of the legs was associated both with cold and with a tuberculous background. The relation of tuberculosis to nodular eruptions of the legs is briefly discussed.

4. A large group of patients showed nodules arising in relation to veins and predominantly hypostatic or phlebitic in character. These correspond to cases described as erythema induratum (Whitfield).

5. A few patients (mostly men) had nodular eruptions associated with thrombophlebitis and erythema nodosum-like eruptions over a number of years and eventually developed arterial disease. The importance of this group is stressed.

6. Finally, the more bizarre features of nodules in association with purpura, ulceration and sometimes more widespread vascular disease are reviewed. These cases probably represent a hypersensitivity reaction, and correspond to "nodular allergides".

7. An attempt is made to distinguish the main features of cases belonging to these different groups.

Much of this work was done as a Senior Registrar in the Skin Department of St. Thomas's Hospital, London.

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CYCLOHEXAMIDE IN THE ISOLATION OF DERMATOPHYTES.

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Cyclohexamide is an antibiotic produced by certain strains of *Streptomyces griseus* ; it has been obtained in crystalline form and its formula determined (Leach, Ford and Whiffen, 1947 ; Ford and Leach, 1948). Under conditions normally employed for streptomycin production the yield of cyclohexamide is poor, but may be greatly increased by suitable adjustment of the medium. The preparation and antibiotic properties of cyclohexamide have been further described by Whiffen (1948). It is a white crystalline powder soluble up to 2% in water, and freely soluble in acetone and butanol ; solutions are stable for several weeks in M/15 potassium di-hydrogen phosphate buffer at pH 3–5 Many yeasts are inhibited by concentrations of cyclohexamide of the order of 0·17 μg./ml. but some require 25 μg./ml. *Candida albicans*, *Coccidioides immitis* and all the dermatophytes are unaffected by concentrations greater than 1000 μg./ml. (Whiffen, 1948). Various species of the common fungal contaminants such as alternaria, aspergillus, fusarium, mucor, penicillium, rhizopus, etc., are inhibited by concentrations of 100 μg./ml. (Georg, 1951). *Cryptococcus neoformans* is highly sensitive to cyclohexamide, which has been used successfully to treat torula meningitis. Georg *et al.* (1951) incorporated cyclohexamide in a penicillin-streptomycin medium and were able to isolate *Coccidioides immitis* from artificially contaminated cultures ; later (1953) she described the use of this medium for the isolation of dermatophytes. In this work the inocula consisted of cattle hairs and of nail clippings which were selected as being heavily contaminated. She obtained more dermatophytes and fewer contaminating fungi on the cyclohexamide-penicillin-streptomycin Sabouraud (CPSS) medium than on the control medium without cyclohexamide.

The investigation here described was carried out in order to decide whether the CPSS medium offered any advantage as a routine medium compared with those at present in use.

In this hospital one of us (D. S.) carries out microscopical and cultural

investigation of all cases of dermatomycosis seen in the dermatological clinic where a total of about 2500 new patients attend yearly; in addition a few cases from other hospitals are investigated. Usually specimens are inoculated within an hour or two of collection and in this way one greatly reduces the incidence of air-borne contamination and obtains a high yield of positive cultures.

The media in routine use are Sabouraud's dextrose agar (SAB) and malt extract tellurite agar (MT) (Riddell, 1951); these have been compared in a small number of cases with the CPSS medium in which cyclohexamide 0·1 mg., penicillin 20 units and streptomycin 40 units per ml. are added to the usual Sabouraud's medium. The penicillin and streptomycin are included to inhibit bacterial contaminants and have no effect on the growth of fungi. Material in which fungus could be demonstrated microscopically was collected from twenty-seven cases of ringworm and divided into three equal portions, so that each of the three media tested was inoculated with an approximately equal amount of material. In every case one or more tubes of each medium were used with three or four inocula per tube. After three weeks the cultures were examined for the growth of dermatophyte colonies, fungal contaminants, and bacterial colonies. The clinical conditions and cultural diagnoses are shown in Table I.

TABLE I.

Source of material:			
Tinea pedis	10 cases	*Trichophyton interdigitale*	5
		T. rubrum	2
		Candida albicans	1
		Epidermophyton floccosum	1
		No growth	1
Tinea capitis	6 cases	*Microsporon canis*	4
		M. audouini	2
Tinea unguium	5 cases	*T. rubrum*	3
		C. albicans	1
		No growth	1
Tinea corporis	2 cases	*T. rubrum*	1
		T. mentagrophytes	1

In addition to the above there was available material sent from Malaya from four cases of tinea imbricata. Although the causal fungus had been readily isolated from a case seen in this country (Sharvill, 1952), previous attempts with Malayan material had proved unsuccessful, the tubes having been invariably overgrown by fungal contaminants.

RESULTS.

Excluding the Malayan cases, the inocula yielded the results shown in Table II. These figures show a slightly larger number of isolations on CPSS

than on the other two media, but much more strikingly, the percentage of inocula yielding contaminant fungi was reduced from 7·8% on SAB and 12·2% on MT to 0·9% on CPSS, the comparable figures for bacterial contaminants being 20·9, 2·6 and 0%. In the Malayan cases, which have been omitted from the table, reduction in fungal contaminants was even more striking. From twenty-one colonies (100%) on both SAB and MT to twelve (57%) on CPSS, with no isolation of *Trichophyton concentricum* on the former two and five isolations on the latter medium.

TABLE II.—*Results of Culturing Material detailed in Table I.*

	Media		
	SAB. No. and % of inocula.	MT. No. and % of inocula.	CPSS. No. and % of inocula.
Dermatophytes	46 (40)	46 (40)	56 (48·7)
Other fungi	9 (7·8)	14 (12·2)	1 (0·9)
Bacteria	24 (20·9)	3 (2·6)	0 (0)
No growth	36 (31·3)	52 (45·2)	58 (50·4)
Totals	115	115	115

The numbers of cultural diagnoses established by the different media are shown in Table III. It is seen that in seven cases (including four of tinea imbricata) isolation was obtained on CPSS only, but that in four cases CPSS failed to grow the causal fungus. The latter were all cases in which only single colonies grew from multiple inocula and the fungi were later shown to be capable of normal growth on CPSS.

TABLE III.—*Cultural Diagnosis* (*including Malayan Cases*).

Medium.	No. of cases.
CPSS and SAB and/or MT	13
CPSS only	7
MT and/or SAB only	4
No fungus isolated	3
Total	27

In none of these cases was there any appreciable difference between the colonies grown on Sabouraud's medium with or without cyclohexamide, either in rate of growth, surface appearance, or pigment production. In several cases slide cultures were set up side by side with and without the antibiotic, and the various conidia and other minute structures appeared identical.

DISCUSSION

In the cases of tinea imbricata the advantage of CPSS was obvious, positive cultures being obtained in three out of four cases, whereas in ten earlier cases no isolation had been made on the usual media.

In the clinic material differences between the media were less evident, SAB and MT each growing 46 and CPSS 56 dermatophyte colonies from 115 inocula. CPSS almost completely eliminated contaminants, both fungal and bacterial, so that it was possible to obtain pure subcultures appreciably earlier than from the usual media.

Under ideal conditions, that is to say where suitably selected fresh specimens are inoculated, and where there is a heavy infection, for example, in most cases of ringworm of the scalp, choice of medium is of little importance. Often, however, isolation is less easy because of scantily infected material, the presence of fungicides, of air-borne contaminants in stale or badly stored specimens, or for other reasons. Such difficulties often arise, particularly in specimens sent to the laboratory by post ; here we normally make multiple inoculations on to two or more different media.

From this limited investigation it appears that the use of CPSS as a sole medium may be justified, especially in reference laboratories or where for any reason a high incidence of contaminated specimens is encountered. Its preparation, although requiring care, is well within the capability of any bacteriological laboratory, and is simpler than that of two separate media such as SAB and MT. Its keeping qualities have not yet been fully investigated, but its properties have been unimpaired by storage for three months at 5° C.

Summary.

Cyclohexamide, penicillin and streptomycin were added to Sabouraud's dextrose agar and the medium compared with plain Sabouraud's agar and with malt tellurite agar.

The medium did not greatly increase the number of dermatophytes isolated from fresh material, but allowed the growth of *Trichophyton concentricum* from heavily contaminated stale material.

In the concentration used there was no obvious effect on the naked eye or microscopic appearances of the fungi studied.

Acknowledgments.

We wish to thank Mr. Winston Anslow of Glaxo Laboratories for gifts of cyclohexamide, Dr. A. C. Cunliffe for help in preparation of this paper, and Mrs. K. Tippett for preparing the media.

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TRANSITION FROM PEMPHIGUS ERYTHEMATOSUS TO PEMPHIGUS VULGARIS: REPORT OF A FATAL CASE PARTIALLY CONTROLLED BY CORTISONE AND ACTH*

HARRY L. ARNOLD, JR., M.D. AND HAROLD M. JOHNSON, M.D.,
Honolulu, Hawaii.

PEMPHIGUS erythematosus, first described in 1925 by Francis Senear and Barney Usher, is now generally agreed to be a relatively chronic and benign variety of pemphigus. It is distinguished from its more severe relative, pemphigus vulgaris, on four principal grounds: (i) Seborrhoeic dermatitis-like lesions of the scalp, face, chest and back, often with thick crusts; (ii) lesions of the face clinically (but not microscopically) imitating lupus erythematosus; (iii) absence of mucous membrane lesions in most cases; and (iv) a relatively mild and chronic course in most cases, with little evidence of systemic illness. Senear himself, with Kingery, reviewed in 1949 the pertinent literature, eliminated the old confusion with lupus erythematosus completely, and stated that a transition could occur from pemphigus erythematosus to pemphigus vulgaris, after which a fatal outcome was much more apt to occur.

In most parts of the world, pemphigus erythematosus seems to be relatively uncommon; Wile and Arnold (1939) were able to find only 43 reported cases in the literature between 1926 and 1938, and in the following four years only 17 probable cases were either reported or presented at dermatological meetings. In Hawaii, however, pemphigus erythematosus seems more common than pemphigus vulgaris; between us we have seen in the past fourteen years 7 cases of the former and only 4 of the latter.

The fact that the symptoms of all forms of pemphigus can often be controlled fairly successfully with ACTH or cortisone or both is generally known. The purpose of this report is to record a case of pemphigus erythematosus in which almost complete control by cortisone and corticotropin combined was achieved with some difficulty, then lost through the patient's negligence, with a consequent relapse which was rapidly fatal despite resumption of treatment with corticotropin and cortisone.

CASE REPORT.

A 47-year-old Japanese housewife was first seen by one of us (H. L. A.) on 6 March 1953 with a rather rapidly progressive vesicular eruption of one month's duration. The lesions were thin-walled blebs 5 to 25 mm. across, confined at first to the scalp,

* Read before the staff meeting of the Straub Clinic, November, 1953.

chest and upper part of the back and later involving the cheeks, forehead, neck, lower portion of the trunk, and proximal limbs. Mucous membrane lesions did not occur. There was no mimicry of lupus erythematosus, but the seborrhoeic distribution, freedom of mucous membranes, absence of systemic symptoms, and thick yellowish-brown crusting of lesions all suggested a diagnosis of pemphigus erythematosus at the time of the first visit. Dr. Senear himself saw the patient in consultation ten days later and agreed with the diagnosis.

The blood count showed only a mild hypochromic anaemia, with a white cell count of 9600 and a normal differential (no eosinophils); urine was normal. Histological examination of a new vesicle showed intraepidermal vesiculation and a nondescript multifocal cellular infiltrate in the corium, consistent with a diagnosis of pemphigus. Chest skiagram showed no disease of lungs or heart. Weight was 9st. 6 lb.

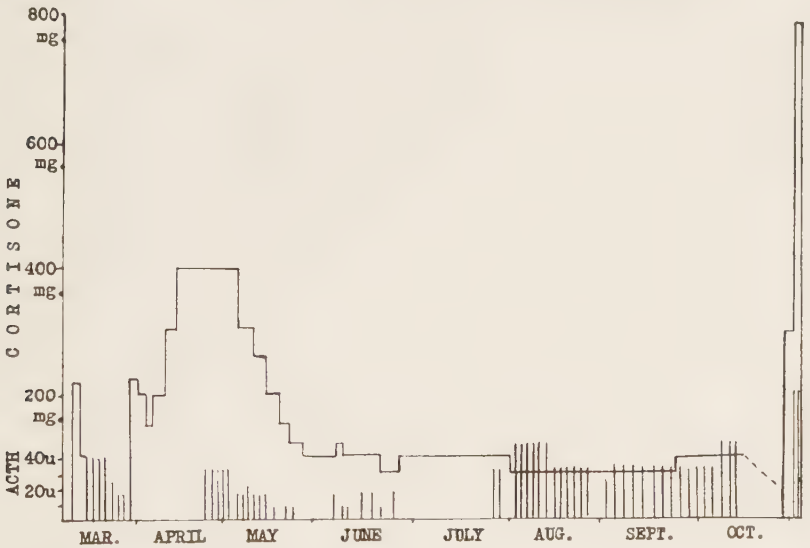

Fig. 1.—Cortisone and corticotropin dosage during the eight months' illness.

Treatment was begun (Fig. 1) with a brief preliminary course of oral cortisone, consisting of 150, 150, 100, 100 and 75 mg. in divided doses on successive days; it was without apparent effect. Ten days later ACTH was begun, 80 mg. daily in the form of the repository gel, with 1 g. of potassium chloride orally, *t.i.d.*; after she had received 80, 80, 60, 60, 40 and 40 mg. on successive days, she was much more comfortable; although visibly oedematous, she had gained only 3 pounds. After four more days, however, it was apparent that no further improvement was taking place, so she was changed to oral cortisone, 75 mg. three times a day, and given triple sulphonamides (1 g.) with penicillin (500,000 O.u.) three times a day by mouth to counteract secondary infection. On the fourth day further healing was apparent and the dose of cortisone was reduced to 50 mg. four times daily. The hypochromic anaemia was no longer present and the blood count now showed 3% eosinophils. Chest skiagram was still normal.

Four days later new lesions had appeared, and when four days of cortisone at 300 mg. a day had not stopped the process, the dose was raised on 14 April to 100 mg. four times a day, supplemented, from 24 April, by 40 units of purified ACTH gel intramuscularly every other day. Not until 4 May was definite healing of lesions

apparent. Blood pressure at this time was 130/60. Oedema was moderate, and rounding of the face was quite marked ; no other evidence of intolerance appeared.

The dose of cortisone was reduced stepwise (Fig. 1) and supplemental ACTH continued, except for an interval from 23 June to 25 July. During this month she was not seen, and became a little worse ; ACTH had to be resumed and increased to 60 units every other day for six doses in order to expedite the healing of the sluggish, crusted lesions of the face and chest especially. Throughout this period the patient was ambulatory, happy, and fairly comfortable.

Early in October the dose of ACTH was again increased to 60 units every other day because of the appearance of a few new blebs. The last dose was given on 10 October, after which she did not return and apparently discontinued oral cortisone of her own volition.

She was next seen by one of us (H. M. J.) on 28 October. At this time she presented huge, heavily crusted erosions involving principally the neck, axillae, inframammary areas, umbilicus, groins and back. Nikolsky's sign was easily elicited. The eyelid margins were heavily encrusted, and there was an erosion of the right buccal mucous membrane. Her temperature was 101° F., and there was a foul odour emanating from the secondarily infected crusts. She was critically ill.

She was admitted to The Queen's Hospital, and cortisone, 100 mg., *t.i.d.* by mouth, was resumed, together with potassium chloride, 1 g. *t.i.d.* Blood pressure was 125/80. The blood count was normal and the urine showed only a few hyaline casts. After the third day, cortisone was raised to 200 mg. *t.i.d.* and supplemented by purified ACTH gel, 40 units twice daily intramuscularly. Permanganate compresses were used locally, since the extensive denudation and the prostration made it impossible to put her into a bath. Penicillin and streptomycin were given intramuscularly to combat the infection.

Her condition slowly deteriorated and she expired on 3 November, the sixth hospital day. Permission for autopsy was refused.

Discussion.

The original diagnosis of this case seems to rest on reasonably secure ground : The seborrhoeic distribution (scalp, chest, upper back and face) from the outset, the absence of mucous membrane lesions during this period, and the absence of systemic symptoms (even malaise) were remarkable, and quite inconsistent with a diagnosis of pemphigus vulgaris.

Remarkable, too, was the amount of steroids required to produce and sustain healing of the skin lesions. Of greatest importance and interest, perhaps, is the severity of the relapse that occurred when she stopped treatment with cortisone and ACTH. It had the appearance of acute so-called " butcher's pemphigus," with raw, oozing erosions in the seborrhoeic areas of the face and body, mucous membrane lesions, and extreme prostration. This outcome did not seem to us to be merely an exaggeration of her pemphigus erythematosus ; we both felt that she had, at the time of this hospital admission, pemphigus vulgaris. The rapidly fatal outcome despite large doses of cortisone and corticotropin suggests that this was so.

Summary.

A case of pemphigus erythematosus in a Japanese woman is described, unusual in that it was controlled only by unexpectedly large doses of cortisone and cortico-

tropin combined, and in that it underwent apparent transition into pemphigus vulgaris within about two weeks of unauthorized interruption of treatment, with a resultant rapidly fatal outcome.

This case strongly supports the generally held view that relapses of serious chronic diseases on discontinuation of steroid therapy may be of more severe degree than the original illness.

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NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

Sheffield, June 1953.

Trichostasis Spinulosa.—Dr. B. M. Buck (for Dr. I. B. Sneddon).

A man aged 23.

History.—Several years' irritating eruption on trunk, shoulders and neck, which started when he was engaged on a very hot job. It is worse in hot weather but does not clear in winter.

On examination.—Brownish follicular papules on trunk, shoulders and neck. Attempted epilation of the follicle produces a plug which under the microscope is shown to consist of 7–10 short lanugo hairs in one bundle.

Histology.—The section shows several hair follicles which contain two or three small hairs within one sheath.

Treatment.—X-ray (500 r) to an area on the back has produced no change in the condition ; application of ung. aquosum with 10% salicylic acid was without effect

? Parapsoriasis and Lesions of the Mucous Membranes.—Dr. H. R. Vickers.

A woman aged 68.

History.—The patient was quite well until 1945 when she first noticed a non-irritating rash in the centre of the lower part of the back.

In 1947 she noticed soreness and ulceration of the buccal mucous membrane. This persisted in spite of various treatments, including intensive vitamin therapy.

In 1951 a skin eruption appeared on the outer aspect of the left thigh and in 1952 on the anterior abdominal wall.

In 1951 she also had for the first time some difficulty in swallowing ; food appeared to stick behind the upper border of the sternum. About this time she also experienced discomfort in the vulva. She was seen in the skin department in April 1952.

On examination (April 1952).—On the lower lumbo-sacral region was a well defined erythematous scaling slightly raised area consisting of grouped follicular hyperkeratotic lesions ; several of these were scattered around the main central plaque which was about 3 in. in diameter. There were similar follicular hyperkeratotic slightly scaling lesions on the anterior abdominal wall and on the outer side of the left thigh.

The tongue was quite smooth and on the inner aspect of the right cheek was a well defined slightly atrophic plaque with superficial ulceration.

Investigations.—Blood count, E.S.R., barium meal and swallow, W.R. and Kahn reactions were all normal.

Histology (21.iv.52).—There is slight hyperkeratosis and a small area of parakeratosis. The rete pegs are well preserved. There is some loosening of the basal cells of the epidermis and a mild chronic inflammatory infiltration of the upper dermis. The appearances are non-specific.

Since April 1952 the patient has been under constant observation. The appearance of the skin lesions has varied, becoming psoriasiform at times. The mouth lesions have remained unchanged in spite of intensive vitamin therapy and avoidance of dentures, and lesions on the vulva, similar to those in the mouth, have appeared.

In May 1953 oesophagoscopy was performed by Mr. A. Young. The tube passed easily through the crico-pharyngeus and nothing abnormal was noticed up to 20 cm., when the lumen narrowed to about 4 mm. This seemed to be a very localized

narrowing. The mucosa above this split and bled a little, as it did at the mouth and the faucial pillar. The lesion in the oesophagus appeared to be of the same nature as that in the mouth.

Barium swallow showed fixity of the oesophageal wall for about 1 in. of its length just above the aortic arch.

Discussion.—In the discussion no members could link the skin and mucous membrane lesions. Psoriasis was suggested by several for the skin lesions.

Twenty-six other cases were shown.

Liverpool, 13 October 1953.

Multiple Ulcers of Unknown Aetiology.—Dr. Glyn Hughes and Dr. McGibbon.

An oxyacetylene welder aged 49 was admitted to hospital on 3 March 1953. His eruption had begun in August 1952 with the appearance of blisters which rapidly increased in size and ruptured to leave indolent raw areas. The elbows were attacked first, then the buttocks and finally the right sole.

Three years before the onset of this eruption, a polyarthritis began in the wrists, spreading thence to the knees and ankles. This proved refractory to treatment with gold, copper and T.A.B.

On examination.—There are extensive areas of ulceration over both elbows and on the buttocks. Smaller ulcers are present on the right foot, under the bases of the first and fifth toes.

Investigations.—E.S.R. (corrected) 16 mm. in 1 hr.

Blood count (on admission): Hb 85%; R.B.C. 4,419,000; W.B.C. 10,000. (Neutros. 39%; lymphos. 54; monos. 7%). Latest W.B.C. 8000. (Neutros. 25%; lymphos. 72; monos. 3%).

Blood W.R. negative.

Examination of scales for fungus, negative. Culture also negative.

Blood culture, sterile after 7 days' incubation. Culture of swabs from elbow lesions, no K.L.B. grown after 48 hours' incubation (contaminants only).

Mantoux 1 : 10,000 negative; 1 : 1,000 positive.

Skiagrams of knees, chest and sinuses were all normal.

Histology.—Appearances are those of a non-specific chronic granulomatous lesion, showing diffuse round celled infiltration of the corium, endothelial and many plasma cells. No acid-fast organisms seen.

Treatment.—Numerous local applications and systemic drugs were administered, including potassium iodide, I.N.A.H. and vitamin B, but none appeared to influence the eruption. A course of intramuscular penicillin was begun, but had to be abandoned on account of prompt urticarial reaction, which took a month to subside in spite of antihistamine therapy. He had previously been found sensitive to chloromycetin also.

For the arthritis courses of sodium salicylate and colchicum were given without appreciable benefit.

Discussion.—Dr. I. B. Sneddon referred to a case of his own presenting similar features. He suggested the possibility that the lesions were the expression of an abnormal reaction to a common organism. In his patient the ulceration had responded temporarily to an antibiotic, but eventually became resistant. Subsequently improvement occurred with x-ray therapy.

Postscript.—In accordance with Dr. Sneddon's suggestion a course of superficial x-ray treatment was given. The ulcers responded by healing centrally, but with peripheral extension.

Reference.

Sneddon, I. B. (1951) *Proc. roy. Soc. Med.*, **45**, 101.

Ocular Pemphigus.— Dr. Freshwater.

A woman aged 72 years.

History.—An eruption of large painful bullae started 4 years ago on the scalp. The bullae, after rupturing, were replaced by crusts, the process giving rise to scarred alopecia with new lesions developing at the edge of the scars. At the same time bullae appeared on the mucous membrane of the nose and mouth and also in the vulval orifice and on the skin of the inner side of both thighs.

Two years ago she developed troublesome lacrimation and soreness of the eyes.

Examination shows a scarred alopecia of the scalp with flaccid bullae at the edge of the scarred area. Bullae can be made out on the conjunctivae of both eyes and these are associated with scarring of the conjunctivae and adhesions.

Histology.—Biopsy of an intact bulla of the scalp shows that the bulla is subepidermal. Owing to technical difficulties it was not possible to obtain a satisfactory biopsy of the mouth lesions.

Progress.—The patient's condition has been slowly progressive and there has been no improvement with treatment with stovarsol and aureomycin.

Twenty-three other cases were shown.

OXFORD REGIONAL DERMATOLOGICAL GROUP.

Northampton, 7 November 1953.

Erythemato-Keratotic Phacomatosis.—Dr. R. B. Coles.

A boy aged 8.

This boy developed scaling and thickening of the skin on his legs and arms shortly after birth, and the condition has persisted since then.

On examination, he shows scaly erythematous areas on the tops of the feet, legs and thighs. The plaques have hyperpigmented borders and have remained constant in outline and character over the last two years. The arms are similarly involved, and there are plaques on both cheeks and on the forehead (Figs 1 and 2). The palms and soles are normal.

Family history.—The patient's father has typical tylosis.

Histology (Dr. W. E. Bryan).—There is a slight degree of parakeratosis with acanthosis. In the superficial part of the corium there is a slight degree of pleomorphic perivascular infiltration. No hair follicles or glandular structures are present in serial sections.

Fig. 1.

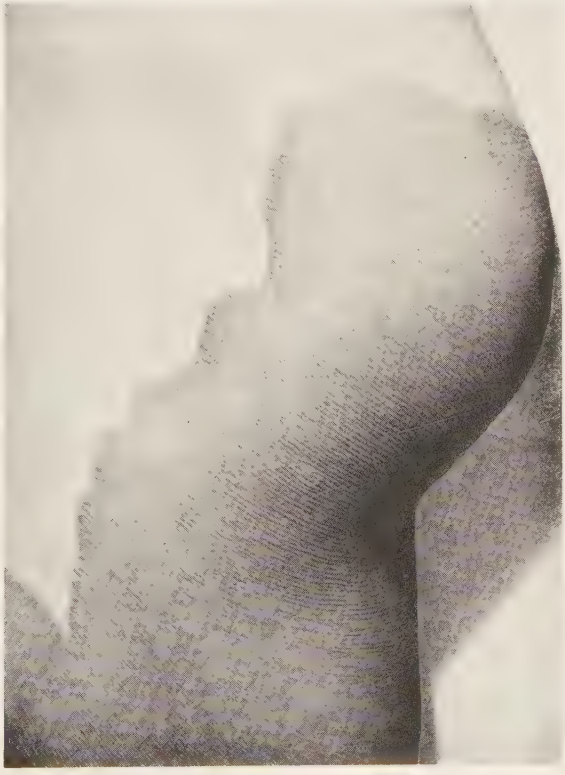

Fig. 2.

Discussion.—This disorder was recently discussed by Gans and Kochs (1951), who mention that Rille used the name of "Keratosis rubra figurata." I have been unable to obtain any record of Rille's cases, but they are said to have been presented at Leipzig in September 1922 (*Hundertjahr-feier deutscher Naturforscher und Arzte*). Mendes da Costa (1925) described a similar condition under the name of "erythrokeratodermia variabilis." He describes a mother and daughter showing this type of epidermal change, but his cases differ, in that their lesions showed constant changes of outline.

Gans and Kochs stress the fixed outline of the plaques and the hyperpigmentation seen around their borders.

Treatment and progress.—Vitamin A 33,000 units was given daily from 26.v.52 until 19.vi.52. He then developed severe purpura for which he was admitted to hospital; attacks of this recurred for about three months. It was thought that this was probably of the Henoch-Schönlein type but since the possibility of vitamin A toxicity could not be excluded this treatment was not continued. During the time that it was given it appeared to have no effect on the eruption.

Thorium X was also without effect.

References.

Gans, O., and Kochs, A. G. (1951) *Hautartz*, **2**, 389.
Mendes da Costa (1925) *Acta derm.-venereol., Stockh.*, **6**, 255.

Seventeen other cases were shown.

CAT.

OBITUARY.

CLARENCE GUY LANE, M.D.

21 October 1882—12 March 1954.

Dr. C. Guy Lane of Boston, Massachusetts, Emeritus Professor of Clinical Dermatology. at Harvard University Medical School, died suddenly aboard ship while homeward bound from a short vacation cruise.

Dermatology will never forget that it owes a great debt to Dr. Lane. for he contributed as much as any other one person to the accomplishments of the last two decades in improving the methods of graduate training in the United States and in establishing the minimum requirements for those who desire to be recognized as specialists in dermatology and syphilology.

But there are many other reasons why Guy Lane will never be forgotten by his patients, his colleagues or his students. For he was a fine physician, an accurate investigator, a sound teacher, and above all a selfless and devoted man. Modest and retiring, he was nevertheless of the most solid and dependable stuff. His unquestioned trustworthiness quite naturally brought to him an unbroken series of great responsibilities, which his colleagues continued to heap upon his slender but capable shoulders. Lane shirked no job ; and every job he took, he worked at to the utmost of his capacities, without fanfare, fuss or feathers. His modesty and his kindness caused him to be loved as well as trusted. It is no wonder then that the following record can include but a fraction of his numerous positions of leadership and of his many contributions.

Born in a small town in the State of Massachusetts, he graduated from Harvard University in 1904 and Harvard Medical School in 1908, to become head of the Department of Dermatology of that School in 1936, Clinical Professor of Dermatology in 1939 and Emeritus Clinical Professor in 1947. In addition to his Chiefship at Harvard's principle teaching hospital, the Massachusetts General Hospital, Lane was consultant dermatologist to no less than eleven other great hospitals in the Boston area.

Dr. Lane's sound contributions to the literature of dermatology and syphilology began in 1910 and continued throughout his life. During these 44 years he contributed over 45 articles and textbook chapters on a very wide range of topics, running the gamut of such subjects as syphilis, tuberculoderms, mycology, roentgenology, military dermatology, industrial dermatology and methods of teaching our specialty. Among his best known works are his very early and original studies of novocain as an occupational contact allergen in dentists ; and his scholarly, critical and practical dissertations on the principles and objectives of postgraduate as well as undergraduate dermatological training.

As the first secretary of the newly founded American Board of Certification in Dermatology and Syphilology from 1932 to 1934 and as its President from 1945–1946, he gained the gratitude and respect of all his colleagues by his untiring and truly invaluable efforts towards the elevation of the standards and quality of our graduate education.

Dr. Lane was member, officer and past-president of many of our leading medical associations, including the New England Dermatological Society, the American Academy of Dermatology and Syphilology, the Section of Dermatology and Syphilology of the American Medical Association and the American Dermatological

Association. He was also honorary or corresponding member of numerous medical societies outside the United States, including the British Association of Dermatology. Among those of his many honours which he prized the most were his selection to be the distinguished lecturer of the Section of Dermatology and Syphilology of the American Medical Association in 1949, and his appointment as Honorary Vice-President of the 10th International Congress of Dermatology in London in 1952.

Educator, investigator and organizer, Dr. Lane was also an accomplished and accurate editor and served upon the editorial boards of many journals including the *New England Journal of Medicine* and the *Archives of Dermatology and Syphilology*.

His hobbies were few and simple, an evening at the movies with his ever-devoted wife, a game of chess or of bridge. One does not need to have first-hand knowledge of his skill at chess or other games to feel quite certain that he not only played them well, but with unfailing courtesy and considerateness for others. For that was the way Guy Lane was made ; and of everything he did, one could truly say : " Well done."

M. B. S.

CURRENT LITERATURE.

FURTHER RESULTS IN THE TREATMENT OF SKIN AND UROGENITAL TUBERCULOSIS WITH ISONIAZIDE. A. Schoch and B. Fust. (1953) *Dermatologica*, **107**, 292.

The authors have had good results from Rimifon (Isoniazide) in lupus vulgaris, tuberculosis colliquativa cutis, tuberculides and erythema induratum. Bladder and genital tuberculosis often responds well, but renal cases commonly fail to improve. In sarcoid striking successes and complete failures both occur. Granuloma annulare does not respond. J. F. S.

SCHISTOSOME DERMATITIS ON THE LAKE OF ZÜRICH. U. Haemmerli. (1953) *Dermatologica*, **107**, 302.

" Bather's itch " has been known in Zürich since 1940, but only in 1951 was its causation thoroughly worked out. Haemmerli in a long and detailed but thoroughly interesting paper describes his investigations on over 500 naturally occurring cases, all from one bathing-station, and particularly among children using a swimming-school there. He also records his studies of 27 experimental infections. He shows how only those swimmers who went within about 60 metres of the solitary snail-bed in the locality were affected, and through his experiments that an initial infection gave rise to quickly-appearing and transient lesions, while subsequent infections gave rise to a delayed, " secondary " reaction lasting for four or five days and much more severe. His histological studies show beautifully how the cercariae die in their burrows in the epidermis, and undergo lysis, while the tissues of the host respond with leucocytic infiltration and oedema. He contrasts this with bilharziasis, in which the parasite, adapted to man, passes through the barrier of the skin unharmed, and provokes little reaction in so doing. An analogous contrast is seen in other infections, e.g., ancylostomiasis and ringworm, where human-adapted parasites provoke little reaction, but those adapted to other species cause much more trouble locally - " creeping eruption " and kerion respectively. Four types of cercariae, all passing one phase of their existence in limnaea ovata, were distinguished. Their end-host is probably a water-bird. As in U.S.A., copper sulphate was found to be the best prophylactic. J. F. S.

THE EXPERIMENTAL PRODUCTION OF "PSEUDOSPIROCHAETES" IN BLOOD. C. G. Schirren. (1953) *Dermatologica*, **107**, 238.

Spirochaete-like forms, often showing apparent spontaneous movement, are frequently seen during the dark-ground examination of preparations containing blood. Some observers have taken these to be actual micro-organisms, but most agree that they are artefacts. Schirren has studied their formation closely by dark-ground and phase-contrast microscopy, and believes that they are formed from the stroma of the red cell, which is first lysed and then precipitated as it

emerges through the damaged capsule of the cell into the surrounding fluid, which has become hypertonic by virtue of the haemoglobin now dissolved in it. He considers that he has gone far to prove this thesis by showing that the addition of a hypertonic solution to a fresh preparation produces numerous "spirochaetes" from every erythrocyte. J. F. S.

THE NEWER DEVELOPMENT OF DERMATOLOGICAL ROENTGEN THERAPY. G. Miescher. (1953) *Dermatologica*, **107**, 225.

Miescher begins by saying that all the additions of the past twenty years to our knowledge of the basic effects of x-rays on the tissues amount to much less than the body of facts previously established, and the fact that most of the work published on this subject deals with doses enormously greater than those used in treating inflammatory dermatoses restricts still further their practical value. Advances in radiotherapy, therefore, are mainly on the technical side, and in the more precise charting of the optimum dose and quality of radiation for particular dermatoses and their changing phases. The tremendously penetrating rays from the Betatron have little to offer the dermatologist, whose special domain is that of the soft rays of low penetration. Until recently there was no apparatus available to span the gap between Bucky's Grenz-rays and the softest rays from the conventional therapy tube, but the beryllium window has now given him the freedom of this important field, and he can choose with considerable precision the wave-length that will reach the desired depth at the desired strength. Older ideas that the harder rays were biologically more effective and selective than the softer have been shown to be untrue, at least within the range employed in practice. The remainder of this long and interesting study gives details of the techniques which Miescher has found best for a wide range of conditions, and does not lend itself to condensation. J. F. S.

THE PROBLEM OF RINGWORM IN NORTHERN IRELAND. *Ulster med. J. Supplement*, 22. 1953.

A rapid increase in the incidence of ringworm in Northern Ireland in 1948 caused to be established, at the Royal Belfast Hospital for Sick Children, a special ringworm clinic which operated between May 1949 and July 1951. The present report surveys the facts and figures obtained during this period. The opportunity is also taken to deal with data from other skin conditions in the province and to present a comprehensive mycological, epidemiological and clinical account. The main value of the work springs from the fact that 427 cases of *M. audouini* ringworm were dealt with, but much valuable information is presented besides. Such a detailed report does not lend itself to summary but is to be regarded as an authoritative and valuable reference for workers in this field. B. A. T.

HOP DERMATITIS IN HEREFORDSHIRE. J. S. Cookson and Ann Lawton. (1953) *Brit. med. J.*, ii, 376.

The incidence of hop dermatitis in Herefordshire in 1952 was about one case in three thousand pickers. Daily observations of 450 pickers showed a much higher incidence of mild dermatitis, for approximately one in thirty developed some type of dermatitis. In some cases sensitivity was shown to be due to fresh hop oil and in three cases sensitivity to hop resins was also present. It is suggested that the rarity of hop dermatitis among workers in dried hops is due to the fact that the sensitizing agent is driven off in the drying process. B. A. T.

SÉZARY'S RETICULOSIS WITH EXFOLIATIVE DERMATITIS. Harold T. H. Wilson and J. Fielding. (1953) *Brit. med. J.*, i, 1087.

A case of exfoliative dermatitis in a subject of chronic eczema is described. Large reticulum cells were found in the peripheral blood. The patient died without developing any of the characteristics of the known reticuloses. The clinical and haematological features were similar to those described by Sézary as a new cutaneous reticulosis, and it is claimed that the case is the first to be reported in this country. B. A. T.

CONTACT DERMATITIS DUE TO AMINOAZOTOLUENE. R. H. Meara and I. Martin-Scott. (1953) *Brit. med. J.*, i, 1142.

Three cases of contact dermatitis due to the aminoazotoluene in coloured semi-solid inks are described. The distribution of the rash and the case histories suggested an exogenous dermatitis; this was proved by patch testing. In two cases the time taken to produce epidermal sensitivity was six to eight weeks, and in the third probably longer. It is suggested that the dye has a low

sensitising index as (at the time of this report) only three cases have so far been published despite the annual sale of two million red and green ball-pointed pens in Great Britain. In the manufacture of the ink there have been no cases of dermatitis among the seventy workers who are exposed each day. B. A. T.

A TRIAL OF GOAT'S MILK IN ECZEMA IN CHILDHOOD. Dennis G. Brown and Roy L. Holman. (1953) *Brit. med. J.*, ii, 1202.

A controlled trial of the therapeutic effects of goat's milk in children with eczema was carried out on nine children, unselected successive admissions to dermatological beds. Under the conditions of the trial, the milk had no effect on the course of the eczema. None of the patients showed cutaneous hypersensitivity with skin tests to cows' or goats' milk. B. A. T.

USE AND ABUSE OF CORTISONE AND CORTICOTROPIN (ACTH) IN DERMATOLOGY. P. A. O'Leary and J. G. Erickson. (1935) *J. Amer. med. Ass.*, **152**, 1695.

An excellent authoritative review, well worth reading. Basing their conclusions on the exceptionally wide experience of the Mayo Clinic, the authors restrict the use of cortisone and ACTH in dermatology to serious or otherwise fatal conditions such as pemphigus and lupus erythematosus, and to self limiting hypersensitivity reactions of severe degree. The results obtained in sarcoidosis, lymphoblastoma, dermatomyositis, scleroderma and acrosclerosis are unsatisfactory. It is possible that cortisone or ACTH may have been responsible for early death from hypertension and renal disease in 6 young women with acrosclerosis. A. J. R.

DECUBITUS ULCERS TREATED WITH DRIED BLOOD PLASMA. A. B. Clark and H. A. Rusk. (1953) *J. Amer. med. Ass.*, **153**, 787.

Decubitus ulcers of 11 patients with spinal-cord injuries were treated with dried plasma to which sufficient Balsam of Peru was added to make a stiff paste. It was difficult to obtain any controls but the results are stated to have been most encouraging. The plasma appeared to clear away the necrotic tissue. A. J. R.

DISSEMINATED LUPUS ERYTHEMATOSUS WITH INVOLVEMENT OF THE SPINAL CORD. P. G. Pier. (1953) *J. Amer. med. Ass.*, **153**, 216.

A girl aged 19 with disseminated lupus erythematosus developed vascular involvement of the spinal cord with infarction and consequent paralysis of the legs. A. J. R.

FATAL APLASTIC ANAEMIA FOLLOWING QUINACRINE THERAPY IN CHRONIC DISCOID LUPUS ERYTHEMATOSUS. L. G. Parmer and A. Sawitsky. (1953) *J. Amer. med. Ass.*, **153**, 1172.

A negro woman aged 36 with lupus erythematosus was treated with quinacrine (mepacrine) gm. 1 twice daily. After 4 months she developed a fatal aplastic anaemia. The authors suggest that the risk of serious reactions of this type may be greater in patients with certain chronic skin diseases than in the general population. A. J. R.

BLASTOMYCOSIS IN TUBERCULOUS PATIENT. A. W. Stillians and H. E. Klemptner. (1953) *J. Amer. med. Ass.*, **153**, 560.

The report of an exceptional case in which pulmonary tuberculosis and cutaneous blastomycosis coexisted. Treatment with streptomycin, iodides and stilbamidine appears to have been effective. A. J. R.

EXFOLIATIVE DERMATITIS FOLLOWING INGESTION OF PHENYLBUTAZONE (BUTAZOLIDIN). H. C. Fishman and J. Reynolds. (1953) *J. Amer. med. Ass.*, **153**, 642.

A detailed report of a case of exfoliative dermatitis in a woman aged 60 which followed the ingestion of 29 200 mg. tablets of Butazolidin. A. J. R.

TREATMENT OF ACTINOMYCOSIS WITH ISONIAZID. L. V. McVay and D. H. Sprunt. (1953) *J. Amer. med. Ass.*, **153**, 95.

Isoniazid was shown to have an inhibitory effect *in vitro* on three strains of *Actinomyces bovis*. Encouraging results are claimed in the treatment of three cases of cervicofacial actinomycosis with this drug. A. J. R.

SOME ENDOCRINE ASPECTS OF SKIN SENSITIZATION AND PRIMARY IRRITATION. III. OBSERVATIONS ON THE INFLUENCE OF COLD EXPOSURE AND FORMALIN TREATMENT (SYSTEMIC STRESS) UPON CUTANEOUS IRRITATION AND SENSITIZATION. Ake Nilzen. (1953) *J. invest. Derm.*, **20**, 185.

Systemic stress of this kind temporarily reduces in guinea-pigs the intensity of cutaneous reactions both to primary and to allergic irritation. A 50% increase in throat size, altered lipoid content, etc., is evidence of the participation of the adrenals.

This reaction, which has also been obtained experimentally in hyperpyrexia, is similar to that which is hoped for in the fever therapy of eczema. It cannot be compared with premedication by corticoadrenal hormones because these, though they may well modify anaphylactic shock and the delayed reaction to tuberculin, have been shown to be quite ineffective for blocking local reactions to histamine or thermal trauma.

The author, having proposed that more information might be secured by similar stress experiments on adrenalectomized animals, goes on to say that when he tried it himself the experiment was frustrated by "increased vulnerability of the animals." He then proceeds to spoil a good argument by urging that the enhanced reactivity, intervening between the reaction we have been discussing and the return to normal, represents a depression of cutaneous resistance. Resistance is a teleological, not a biological, conception, and its definition should be limited to reports on B.I. 161. J. H. T. D.

OBSERVATIONS ON PERIPHERAL CIRCULATION IN PSORIASIS. Stanley E. Huff and Henry Longstreet Taylor. (1953) *Arch. Derm. Syph., Chicago*, **68**, 385.

Changes in the blood content of the finger tips with each heart beat have been studied with a photoelectric plethysmograph in 28 normal subjects and 11 patients with psoriasis. The tracings from the latter were considered abnormal, "additional evidence of a vascular dysfunction in patients with psoriasis." J. K.

CORRECTIVE SURGICAL PLANING OF THE SKIN—NEW TECHNIQUE FOR TREATMENT OF ACNE SCARS AND OTHER SKIN DEFECTS. Abner Kurtin. (1953) *Arch. Derm. Syph., Chicago*, **68**, 389.

This modification of the sandpaper method uses rapidly revolving wire brushes. While the results are claimed to be good "it may take several hundred planings before the operator can develop a sense of dexterity and security." This is only one disadvantage of this procedure; another is the possibility of persistent skin irritability caused by too many operations, which has been reported after sandpapering. J. K.

CORRELATION OF RATE OF GROWTH WITH HISTOLOGIC CHARACTERISTICS OF BASAL CELL CARCINOMATA. Henry A. Teloh. (1953) *Arch. Derm. Syph., Chicago*, **68**, 408.

This study of 100 cases of basal cell carcinoma is an attempt to correlate degree of malignancy with histological characteristics. Unfortunately, beyond the fact that a greater degree of inflammation and centrifugal invasion was noted in rapidly growing tumours the findings had no statistical significance. J. K.

AXILLARY ODOUR—EXPERIMENTAL STUDY OF THE ROLE OF BACTERIA, APOCRINE SWEAT, AND DEODORANTS. Walter B. Shelly, Harvey J. Hurley and Anna C. Nichols. (1953) *Arch. Derm. Syph., Chicago*, **68**, 430.

Apocrine sweat is odourless. The distinctive odour is produced by the action of organisms and it is increased by the presence of hair which retains secretions and bacteria. Intensive use of hexachlorophene-detergent preparations will abolish the odour for 18 hours but shaving and washing for 24. J. K.

CONTRIBUTIONS TO THE STUDY OF PEMPHIGUS. Joseph G. Brennan. (1953) *Arch. Derm. Syph., Chicago*, **68**, 481.

The author confirms the value of the Tzanck test in pemphigus. He finds that in bullae produced by cantharides on apparently normal skin of pemphigus patients the same acantholytic cells are seen, while in other bullous diseases and in normal persons they are not found if the examination is made 3 hours after the cantharides is applied. If examination is delayed beyond this time acantholysis might be seen in some patients not suffering from pemphigus. J. K.

LOW INCIDENCE OF DERMOGRAPHISM IN SUBACUTE AND CHRONIC URTICARIA. A. A. Fisher and Sidney Schwartz. (1953) *Arch. Derm. Syph., Chicago*, **68**, 553.

Dermographism was present in 5 out of 100 dermatological patients with no urticaria and in 6 out of 100 with urticaria. In 19% of the cases of chronic urticaria allergic factors could be found but not in any case of dermographism. J. K.

CHRONDRODERMATITIS NODULARIS CHRONICA HELICIS—REPORT OF NINETY-FOUR CASES AND SURVEY OF LITERATURE, WITH EMPHASIS UPON PATHOGENESIS AND TREATMENT. Victor D. Newcomer, Charles George Steffen, Thomas H. Sternberg and Louis Lichtenstein. (1953) *Arch. Derm. Syph., Chicago*, **68**, 241.

The article expands the title to some ten pages including illustrations but the explanation of the cause of the condition is not convincing and the results of treatment disappointing. J. K.

DERMATITIS OF THE HANDS—ETIOLOGY AND PRINCIPLES OF TREATMENT, WITH OBSERVATIONS CONCERNING A HYPERKERATOTIC DERMATITIS OF THE VOLAR SKIN. Richard L. Sutton, Jr. and Samuel Ayres, Jr. (1953) *Arch. Derm. Syph., Chicago*, **68**, 266.

A paper by either author is always worth reading and this joint one doubly so, especially perhaps, for the points on which they cheerfully agree to differ. It deals adequately and without padding on the aetiologically heterogeneous but often clinically similar conditions, with sensible lines of treatment, including, of course, elimination of focal sepsis. The condition specially mentioned in the title is that described by Mary Smith (*Brit. J. Derm.* (1942), **54**, 255) to whom they give due credit. J. K.

FLUORESCENCE OF MICROSPORUM INFECTED HAIR—II. CULTURAL STUDIES. Harry M. Robinson, Jr., Frank H. J. Figge and Eugene S. Bereston. (1953) *Arch. Derm. Syph., Chicago*, **68**, 311.

The authors have failed to produce fluorescence on artificial media. They point out that fluorescence in hair is not necessarily evidence of a viable fungus and that hair kept till the fungus has died out still fluoresces. J. K.

INVESTIGATIONS ON PATHOGENIC FACTORS AND TREATMENT OF TINEA UNGUIUM. H. Goetz. (1953) *Arch. Derm. Syph., Berl.*, **193**, 579.

A mixture of sodium thioglycolate, sodium iodide and 8 oxy-quinoline in a tylose mucilage at pH 7·8–8 softens the nail so that it can be easily scraped away and it is an effective fungicide. The results in a clinical trial are in the nature of a preliminary report. M. F.

ON DISSEMINATED ECZEMATOID MICROBIDES. R. Strempel. (1953) *Arch. Derm. Syph., Berl.*, **193**, 650.

When a localized focus of eczema, usually on the lower limb, is treated with unsuitable medicaments and a secondary "ide" eruption results on other parts of the body this is often the result of the development of a sensitization to skin organisms, usually staphylococci. M. F.

HYALINOSIS CUTIS ET MUCOSAE (LIPOID-PROTEINOSIS (WIETHE-URBACH)). W. Braun and H. Weyhbrecht. (1952) *Arch. Derm. Syph., Berl.*, **194**, 548.

The trouble is regarded as a paraproteinosis. The hyaline collections in the dermis have a reduced lipoid content. Electrophoresis shows increase in α and β globulins. There is increased aminoacid excretion (especially tyrosine) in the urine. M. F.

AETIOLOGY AND THERAPY OF ONYCHOGRYPHOSIS. H. R. Fischer. (1953) *Arch. Derm. Syph., Berl.*, **193**, 661.

Onychogryphosis is not so much a separate entity as the effect of various diseases or trauma upon the growth of the nail. Eczema, psoriasis, varicose ulcer and tinea were found in one quarter of the cases. M. F.

HAEMANGIOMATOSIS MULTIPLEX SARCOMATOSUM (KAPOSI). G. Klein. (1952) *Arch. Derm. Syph., Berl.*, **194**, 527.

A case affecting the face, trunk, upper extremities and internal organs in a 76-year-old woman. The process is considered to be a benign tumour of blood vessels, a hamartoma. In spleen and liver were found multiple malignant configurations, reminiscent of a sarcomatous haemangio-endothelioma. M. F.

MELANOSARCOMA OF SKIN. H. A. Gottron and W. Nikolowski. (1952) *Arch. Derm. Syph., Berl.*, **194**, 519.

A small bluish hemispherical tumour in the gluteal region of a 37-year-old man, the histology of which showed resemblances to and differences from blue naevus leading to a diagnosis of a melano-fibroplastic sarcoma. There was no evidence of metastasis. M. F.

BIOLOGICAL OXYDATION OF HUMAN SKIN. I. v. Glasenapp and G. Leonhardi. (1953) *Arch. Derm. Syph., Berl.*, **196**, 319.

By using the appropriate enzyme inhibitors, the course of glycolysis, the citric acid cycle, oxidative phosphorylization and the cytochromeoxydase-cytochrome system were investigated. Oxidative processes were the same in human skin as in other organs. M. F.

INVESTIGATIONS ON URTICARIA. E. Muller. (1953) *Arch. Derm. Syph., Berl.*, **196**, 375.

In 80 cases of urticaria, an allergic basis dependent upon foodstuffs, medicaments, focal infection, worms and insects, was found in no less than 55%. In some of the other cases psychogenic, physical or hormonal factors appeared to be important. M. F.

FREE AMINOACIDS IN CANTHARIDES BLISTER AND SERUM. W. Adam and G. W. Korting. (1953) *Arch. Derm. Syph., Berl.*, **196**, 325.

Paper chromatography showed the same values in artificial blister and serum. M. F.

SYMPTOMATOLOGY, LOCALIZATION, AGE AND SEX DISTRIBUTION OF NAEVUS VASCULOSUS OSTEOHYPERTROPHICUS. (Klippel-Trenaunay-Parkes Weber Syndrome.) E. Petschelt. (1953) *Arch. Derm. Syph., Berl.*, **196**, 155.

Two case reports and a review of the literature of 50 other cases. Men are affected more often than women. The upper extremity is more frequently involved than the lower in men, but equally in women. Aetiology is uncertain. M. F.

CLINICAL AND EXPERIMENTAL INVESTIGATIONS ON THE AFTER EFFECT OF ANTI-ECZEMATOUS MEASURES. G. G. Jagtman. (1933) *Arch. Derm. Syph., Berl.*, **196**, 137.

Atopic dermatitis is being considered. While in hospital one half of the body was treated with active medicaments, the other side served as control. Relapse occured earlier on the control side. Tar in the form of "liantral" paste was most effective, chrysarobin (tolerated better than in psoriasis) next, then liquor picis detergens, oleum rusci only slightly, resorcin and phenol only little. Sulphur on the other hand seemed to predispose to earlier relapse. M. F.

INVOLVEMENT OF BONE IN MYCOSIS FUNGOIDES. H. Reich and G. Bonne. (1953) *Arch. Derm. Syph., Berl.*, **196**, 176.

An x-ray of the pelvis of a patient in the tumour stage of mycosis fungoides showed spontaneous fractures and areas of osteoporosis. After x-ray treatment the bone seemed to consolidate rapidly. Lymph node enlargement now took place and the histology was that of reticulum-cell sarcoma. M. F.

CHOLESTEROL METABOLISM OF HEALTHY AND PSORIATIC SKIN. J. v. Glasenapp and G. Leonhardi. (1953) *Arch. Derm. Syph., Berl.*, **196**, 148.

Values are given for total fat, free cholesterol, cholesterol esters and phospholipid content of normal skin of patients between the ages of 30–40, for epidermis and cutis. The healthy epidermis of psoriasis patients shows the same values. Psoriasis papules have increased total cholesterol and free cholesterol, probably the result and not the cause of the tissue change. M. F.

SPIEGLER CYLINDROMA AND EPITHELIOMA ADENOIDES CYSTICUM BROOKE. E. H. Graul. (1953) *Derm. Wschr.*, **128**, 949.

A father and daughter had many Spiegler's cylindromata (of scalp particularly) : the daughter had also mild epithelioma adenoides cysticum of the face. The daughter's involved brow at the frontal margin was treated with contact x-ray therapy. 60 kV ; 6 mA ; FSD 5 cm. ; daily doses of 300–500 r ; total dose 6000 r. Nine months after therapy there was no histological evidence of the tumour and the cosmetic result was still excellent when seen $2\frac{1}{2}$ years later. A mother and daughter with epithelioma adenoides cysticum (Brooke) are also described. As the histology resembled so closely that of Spiegler's cylindroma and the two conditions may be present simultaneously as in the patient described, contact x-ray treatment was given to the daughter (300–400 r daily ; total dose 6500 r) leading to an epithelitis : $3\frac{1}{2}$ years later the cosmetic result was so good that the mother decided to have the same treatment. Photographs and photomicrographs illustrate the text. M. S. S.

CLINICAL AND EXPERIMENTAL INVESTIGATIONS ON THE ACTION OF AMMI MAJUS ON PIGMENT METABOLISM AND THEREBY ON THE TREATMENT OF VITILIGO. G. W. Korting, H. C. Friederich and W. Adam. (1953) *Derm. Wschr.*, **128**, 934.

Of 5 vitiligo patients treated locally and orally with meladinine (which contains ammoidine and ammidine) 3 developed a bullous eruption over the patches following unintentionally longer exposure to sunlight (artificial or natural) ; there was no meladinine on the skin at the time of exposure. In 2 patients the bullae appeared within 2–3 hours, in the other after 24 hours. In only 1 of the 5 patients (one of the others) was there satisfactory repigmentation and this appeared first in the spring following exposure to natural sunlight. From animal experiments the authors conclude that the action of the drug is due to photodynamic sensitization, not to a direct action, through the enzyme system (tyrosine-tyrosinase) on pigment metabolism. M. S. S.

THE DISTRIBUTION OF POLYSACCHARIDES IN THE EPIDERMIS IN DERMATOSES WITH ACANTHOSIS. O. Braun-Falco. (1953) *Derm. Wschr.*, **128**, 1021.

The dermatoses include neurodermatitis, psoriasis, erythematodes, pemphigus, dermatitis herpetiformis, papilloma and lichen planus. By histochemical methods Schiff-positive polysaccharides (glycogen in particular) were found as a rule in the middle of the acanthotic prickle cell layer (apparently particularly when oedematous) but not in the basal, granular or corneous layer except in the presence of parakeratosis when they were found in the parakeratotic areas.

The author considers that in the absence of a well-marked granular layer the polysaccharides fail to become synthesized into the lipoids necessary for normal cornification.

In spino-cellular carcinoma Schiff-positive substances are found (in increased amount) but not in basaliomas. It is of interest that two types of cases are said to show opposite behaviour in their arginase activity. In basaliomas, seborrhoeic warts, etc., with basal cell proliferation there is no increase in arginase activity ; where there is a rete cell proliferation on the other hand, e.g., in psoriasis, common warts, etc., there is increased arginase activity. M. S. S.

PAPULAR TUBERCULIDES AFTER BCG VACCINATION. J. I. De Buyne, S. Van Creveld, J. R. Prakken, and M. R. H. Stoppelman. (1953) *Acta derm.-venereol., Stockh.*, **33**, 385.

Papular tuberculides occurred in 5 infants after BCG vaccination. Three months after vaccination small brownish red nodules, like lupus vulgaris seen by diascopy, appeared at the injection site. Also brown yellow glistening firm pin-head or lental papules formed an extensive eruption on face, cheeks, trunk and extensor aspect of extremities ; some papules were covered with a tiny scale, but no necrosis occurred. Tuberculin test 1/1000 was positive and in all cases the eruption disappeared without scarring within 2–3 months. G. A. H.

STUDIES OF THE PERIPHERAL WHITE BLOOD COUNT IN GUINEA PIGS SENSITIZED TO 2 : 4 DINITROCHLORBENZENE. G. Seeberg. (1953) *Acta derm.-venereol., Stockh.*, **33**, 359.

In guinea-pigs sensitized to 2 : 4 dinitrochlorbenzene the granulocyte count increased 5–7 hours after re-exposure to the same chemical ; no comparable increase occurred in the lymphocyte count. G. A. H.

RELATION BETWEEN PSORIASIS AND POLYARTHRITIS. H. F. H. Reiter and A. Norholm-Pedersen. (1953) *Acta derm.-venereol., Stockh.*, **33**, 372.

Psoriasis does not occur more often in polyarthritis cases than in a control series, but patients with extensive psoriasis are more liable to affections with polyarthritis than those with more circumscribed forms and an active polyarthritis often determines a more universal and atypical extension of the psoriasis. The prognosis is poor for polyarthritis cases with extensive and atypical psoriasis. G. A. H.

CONTRIBUTION TO THE TREATMENT OF LEPROSY. O. Gans. (1953) *Ann. Derm. Syph.*, **80**, 345.

The author describes his experiences in India in treating leprosy with methylene blue. He thinks that this method is of definite value and more so if associated with copper salts. F. F. H.

A FATAL CASE OF LUPUS ERYTHEMATOSUS TREATED WITH ATEBRINE. X. Vilanova and J. M. de Moragas. (1953) *Ann. Derm. Syph.*, **80**, 360.

A woman of 73 with lupus erythematosus was treated with atebrine, receiving 8g. in 55 days, after which she died of agranulocytosis. F. F. H.

PLATELET ANTIBODY TESTS IN THE DIAGNOSIS OF PURPURA. J. L. Tullis. (1953) *New Engl. J. Med.*, **249**, 591.

This article is concerned only with thrombopenic purpura, and the test described is to discover those cases in which a circulating antibody is responsible for the thrombopenia. This knowledge is important not only for diagnosis but because it may affect treatment. Patients whose symptoms are due to allergen-antibody reaction are likely to benefit from ACTH and cortisone, but not from platelet transfusion.

The test itself is incubating a mixture of preserved platelets, human complement and unknown serum at 37° C. and examining it for quantitative changes in total count after forty-five and ninety minutes. A. D. P.

THE EFFECT OF ANIMAL AND PLANT PEPTONES ON THE DEVELOPMENT OF THE PIGMENT OF TRICHOPHYTON PURPUREUM. E. Grunberg and E. Titsworth. (1953) *J. invest. Derm.*, **20**, 197.

Animal peptone gives a better colour. The superficial appearance of the colonies of *Paracoccidioides cerebriformis* is also influenced by the quality of the peptone. The other fungi tested did equally well with all sorts. The work also confirms the observations of Lewis and Hopper (1941) on sugars. J. H. T. D.

SUPEREGO AND AGGRESSION IN CIRCUMSCRIBED NEURODERMATITIS. P. F. D. Seitz, J. S. Gosman and J. Craton. (1953) *J. invest. Derm.*, **20**, 263.

A not particularly successful attempt to measure the superego in feet and inches, and to provide evidence that neurodermatitis may be an expression of ingrowing exasperation.

In the discussion attention was called to the circumstance that many patients, with what has been called neurodermatitis, might merely be trying to live up to the explanations supplied by their doctors; also to the therapeutic superiority of those forms of suggestion the content of which is not painstakingly explained to the patient. Do we not write our nipsochrismatic formulae in Latin and illegibly, or else leave it to the pharmacist to supply the unknown?

The selection, as controls, of patients suffering from itching non-lichenified dermatoses was criticized, but surely on the wrong grounds. For is not the faculty of lichenification merely incidental to the desire to scratch? J. H. T. D.

GRENZ-RAY THERAPY IN CUTANEOUS DISEASES. U. Leitner. (1952) *Med. Pr.*, **227**, 112.

Since Grenz rays are almost completely absorbed in the first 3 mm. of the skin they can be used repeatedly without any risk of serious damage.

The results of treating 363 patients suffering from a variety of dermatoses are tabulated and briefly discussed. H. R. V.

COMPARATIVE STUDIES IN THE TREATMENT OF ACNE VULGARIS UTILIZING INTRADERM SULPHUR AND INTRADERM TYROTHRICIN. R. O. Noojin and J. W. Sewell. (1951) *J. invest. Derm.*, **16**, 261.

The difficulties of assessing results of treatment in acne vulgaris are formidable. While the course of the disease can be recorded by means of photographs, anybody who took the trouble to do this would be saved the trouble in future of worrying what treatment to prescribe—and that would be bad for trade. But in this series of 184 consecutive patients the assessment of results was based on merely asking the patient how she liked it.

The only information about the mode of selection is that one whole treatment group consisted of a single sex and class—student nurses. It is not stated that the other treatments were allotted in turn to consecutive patients; indeed the differing totals indicate that they were not. Many of the patients were over 21. Had this experiment yielded statistically significant results they would have been invalidated by suspicion of conscious selection.

While it is true that the life of the individual papule may be 3–6 months—longer than those of us who have not made the observation would imagine—any effective treatment must either prevent the formation of fresh papules or it must accelerate the involution of those already present. Neither phenomenon was specifically noted. J. H. T. D.

SPECTROPHOTOMETRY OF LIVING HUMAN SKIN IN THE ULTRAVIOLET RANGE. E. A. Edwards, N. A. Finkelstein and S. Q. Duntley. (1951) *J. invest. Derm.*, **16**, 311.

Spectrophotometry has of course the last word in defining a given colour in that it measures the quantity of light reflected and absorbed in each part of the spectrum without the intervention of human judgment.

If we measure with a photoelectric cell the light reflected from equal areas of freshly prepared magnesium oxide and of a coloured surface, both of them illuminated by a beam of the relevant hue, we shall get an answer in terms of their comparative reflectancy or "value." A comparison between the reflectancy of white light and of light having the same hue as the sample would measure the intensity or "chroma" of the colour, but in the method described this dimension is calculated indirectly. If we use the whole spectrum taking in turn each wave-band, the width of which depends on the type of instrument, we get a series of readings forming a curve from which we can deduce the hue, its chroma and value or, to use the terminology of this article, its intensity, purity, shade and tint.

The Hardy spectrophotometer, which is employed for measurements within the visible spectrum, automatically provides such a continuous curve. The Harrison instrument, the only one available for measurement in the ultraviolet range, yields a series of dots which, having considerable scatter when illumination is faint, must be joined up by hand. This spectrophotometric curve in spite of its limitations does more than simply register the hue, chroma and value of the light reflected; for it also displays secondary curves representing the characteristic absorption bands of such substances as reduced and oxy-haemoglobin, carotene, vitamin A, etc.

Unfortunately both the particulate melanin and soluble melanoid absorb uniformly throughout the whole visible and ultraviolet spectrum and thus obscure the other things we might wish to look for—for instance haemofuscin in the negro. Moreover the scattering produced by the turbidity or opalescence of the rete, which is of course responsible for the blueness of shaved chins, veins and monkeys' bottoms, also interferes with identification. Nevertheless no attempt accurately to define the colour of the skin should be despised by the dermatologist.

J. H. T. D.

GAMMA-GLOBULINS IN DERMATOLOGY, THEIR CLINICAL AND THERAPEUTIC IMPORTANCE. G. Scotti. (1953) *Dermatologia*, **4**, 23.

A review of the state of our knowledge about globulin-level changes in skin disease, and a discussion on the possibility of its wider therapeutic use. Panzera has used it in a case of pemphigus, apparently with some success. D. S. W.

THE OCCURRENCE OF THE DERMATOPHYTE, MICROSPORON GYPSEUM, AS A SAPROPHYTE IN SOIL. M. A. Gordon. (1953) *J. invest. Derm.*, **20**, 201.

One method of studying the bacterial flora of the soil consists of stirring up a sample with normal saline, allowing the suspension to stand for 2 hours, and then filtering the supernatant fluid through a membrane on the surface of which the microbes can be stained with McManus and examined under the microscope. While scanning for *Histoplasma capsulatum* the author

happened to detect a few spores of (macroconidia) *M. gypseum*. He subsequently succeeded in isolating the fungus from the same sample.

It appears that one can also fish for *M. gypseum* by burying strips of flannel in the ground as bait. But it is no doubt in accordance with nature that schoolboys' caps would succumb to wear and tear or to the ravages of the other kind of *tinea* long before they would have time to be devoured by the microsporon. J. H. T. D.

SOME EFFECTS OF ACTH CORTISONE PROGESTERONE AND TESTOSTERONE ON SEBACEOUS GLANDS IN THE WHITE RAT. D. Haskin, N. Lasher and S. Rothman. (1953) *J. invest. Derm.*, **20**, 207.

Testosterone enhances growth and secretion of the sebaceous glands : oestrogen reduces them and the two hormones neutralize one another in this respect. Progesterone does not produce acne in females with normal ovaries.

Androgens of adrenal origin are supposed to cause acne in adolescent girls, but not only normal males but eunuchs and " most ovarian deficient females " can have excellent adrenals without developing acne.

The acne produced by ACTH is said to differ from juvenile acne in that oily seborrhoea is lacking and the follicular hyperkeratosis does not produce true comedones. Moreover older women tend to grow facial hair instead. That this is not due to a reversal of follicular function is attested by those males from whose acne neither beards nor middle age bring respite.

Serial sections were made of the skin of spayed rats, which have very small sebaceous glands, both before and after treatment with daily doses for a month of cortisone 1 mg., ACTH 0·5 mg., testosterone 2 mg. or progesterone 10 mg. ; and the increase in volume of the sebaceous gland was carefully measured by projection of the slides on a screen ruled in squares. Testosterone and progesterone (10 mg.) both gave about 500% increase : ACTH and progesterone (1 μg.) each not quite 100%. The natural hair-growth cycle of the rat was not taken into account.

J. H. T. D.

***IN VITRO* STUDIES ON THE FUNGISTATIC EFFECT OF ANTIHISTAMINIC DRUGS.** W. J. Fahlberg. (1953) *J. invest. Derm.*, **20**, 171 ; and **RELATION OF CHEMICAL STRUCTURE TO FUNGISTATIC ACTIVITY.** A. I. Chinn, R. B. Mitchell and A. C. Arnold. (1953) *J. invest. Derm.*, **20**, 177.

Certain antihistamines applied to the surface of seeded plates and added to broth cultures of various fungi were found to inhibit growth. The effects were unequal both between the different antihistamines and the fungi.

Antihistamines having a halogen in their phenolic nucleus are more fungistatic than those without. For example benadryl itself is only weakly fungistatic whereas two nameless chlorinated forms of it are highly effective. J. H. T. D.

THE EFFECTS OF CORTISONE ON EXPERIMENTAL COCCIDIOIDOMYCOSIS. V. D. Newcomer, E. T. Wright, J. E. Tarbet, L. H. Winer and T. H. Sternberg. (1953) *J. invest. Derm.*, **20**, 315.

It remains doubtful if cortisone has any effect adverse or otherwise on the survival of mice infected with *Coccidioides immitis*. J. H. T. D.

CLINICAL AND EXPERIMENTAL STUDIES WITH 8-METHOXYPSORALEN IN VITILIGO. A. B. Lerner, C. R. Denton and T. B. Fitzpatrick. *J. invest. Derm.*, **20**, 299.

Ammoidin majudin and ammidin were local names for xanthotoxin bergapten (*bergamot*) and imperatorin but these, again, are botanological synonyms for 8-methoxypsoralen 5-methoxypsoralen and 8-isoamyleneoxypsoralen (*Psoralea corylifolia*). While the crude plant *Ammi majus* Linn. (will somebody please show us quickly what it looks like !) has been used with complete success for the production of repigmentation, coma, nephritis, hepatic cirrhosis and exfoliative erythrodermia since the days of the Pharaohs, the refined product yielded only one complete satisfactory result in the short series CISIISSSS (cured, improved, the same) and no appreciable disturbance of metabolism except that which is indicated by the cephalin cholesterol flocculation test. Applied locally the drug enhances inflammatory as well as pigmentary reactions of the skin to light but ingested it may improve tolerance of light in extensive cases of vitiligo and in albinos.

This exhaustive pharmacological study will supply most of the answers to those interested but the clinical results promise little of practical value. J. H. T. D.

THE EFFECT OF CYSTEINE HYDROCHLORIDE ON RADIATION-INDUCED DEPIGMENTATION OF MOUSE HAIR. M. H. Kulwin. (1953) *J. invest. Derm.*, **20**, 237.

It is now accepted that x-rays act on tissue by ionization of the water in them, rather than by a disturbance of the structure of individual molecules by the impact of photons. Hence an enzyme in dilute solution, or with something added to the solution to compete with the products of hydrolysis, sustains more damage than when concentrated. Similarly seeds and spores undergo more alteration by x-rays if they are moistened than when they are dry.

In the biochemistry of oxidation and reduction, protein substances with free –SH groups are just now supposed to be the thing. This is why the uncongenial cysteine was chosen for administration in various ways to mice in order to explore the possibilities of chemical protection of tissues against radiation. Can the skin be protected by inunction of –SH containing materials while the radiologist does his worst to the thyroid, or can the bone-marrow be protected by intravenous injection of a selective antidote while we try to get rid of the mycosis fungoides on the skin?

But cysteine is an irritant and it prevented its own absorption through the peritoneum by inflaming it. Injected into the skin it was suspected of neutralizing the greying effect of x-rays on the hair merely by the hyperpigmentation that accompanies any banal inflammation.

J. H. T. D.

STUDIES OF METHODS OF DETERMINING CAPILLARY FRAGILITY. II. NEGATIVE PRESSURE TECHNIQUE USING THE "PETECHIOMETER." D. J. Perry and I. H. Linden. (1953) *J. invest. Derm.*, **20**, 257.

The petechiometer is a transparent suction cup with a device for producing different negative pressures in it.

Its measurement of capillary fragility is unsatisfactory in the upper extremity and the infraclavicular regions because of great differences between left and right in the same individual. The back is no good because the values are too low, nor the legs because they are too high. Even if some part of the body could be found to yield consistent results with a practical range of values, the effects on capillary fragility of temperature, barometric pressure, allergy and the menstrual cycle are insufficiently known for their importance to be taken into proper consideration.

J. H. T. D.

THE EXPERIMENTAL PRODUCTION OF LEUCOCYTIC CHANGES IN NORMAL BLOOD, SIMILAR TO L. E. CELLS AND MORPHOLOGICALLY IDENTICAL WITH L. E. CELLS. J. Inderbitzin. (1953) *J. invest. Derm.*, **20**, 67.

Treatment of blood *in vitro* with certain substances of high molecular weight and described as anticoagulants brought about phagocytosis of leucocytes. Polyanetholsulphonic acid produces, independently of any serum factor, phagocytosis of clumped thrombocytic masses. The sodium salt of polyvinyl alcohol polysulphonic ester requires the presence of gamma globulin in order to produce any effect at all: but, heated to 55° C. with serum it causes the appearance of L.E. cells indistinguishable from the genuine article. The author speculates on the possibility that the L.E. phenomenon may be caused by the presence in the circulation of mucopolysaccharides derived from damaged collagen.

J. H. T. D.

LICHEN MYXOEDEMATOSUS (DIFFERENTIATION FROM CUTANEOUS MYXOEDEMAS OR MUCOID STATES). H. Montgomery and L. J. Underwood. (1953) *J. invest. Derm.*, **20**, 213.

In this disorder either multiple discrete or more diffuse deposits of mucin in the skin produce a highly variable clinical picture. There is no appreciable dysfunction of the thyroid nor indeed any specific involvement of other systems. The single autopsy failed to reveal muscle changes in a patient who had not been able to open his mouth or put on his coat and who suffered from cramp when he tried to walk.

The pathogenesis of the malady is discussed with special reference to its affinities with lichen amyloidosus, calcinosis, granuloma annulare, dermatomyositis and scleroderma. 70 references to the literature are given.

J. H. T. D.